VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF DIABETES MELLITUS (DM) IN PRIMARY CARE

Guideline Summary

RECOMMENDATIONS WITH THE HIGHEST EVIDENCE: The highest evidence for recommendations is A, defined as "a strong recommendation based on randomized controlled trials that the intervention is always indicated and acceptable."

The following practices are strongly recommended based on evidence reviews:

- 1. For patients with very mild or no microvascular complications of diabetes, and those free of major concurrent illnesses and with a reasonable life expectancy, the HbA₁c target should be < 7 percent. [R=A]
- 2. Initial monotherapy with a sulfonylurea or biguanide (i.e., metformin) should be used as first-line drug therapy. Sulfonylurea can be considered for most patients with type 2 diabetes; however, for those who are significantly overweight (body mass index [BMI] > 25), initial monotherapy with a biguanide may be preferable. [R=A]
- 3. In patients treated with **large doses of insulin**, addition of a thiazolidinediones (TZD) may reduce the insulin requirement and produce improved glycemia, with reduction of HbA₁c by 1 percent. [**R**=**A**]
- 4. The use of insulin lispro or glargine is not recommended for routine use in the treatment of type 2 DM, as there is no evidence that it has any inherent superiority to more established insulin preparations in lowering HbA₁c levels. [**R=A**]
- 5. Patients with impaired glucose tolerance (IGT) (i.e., a fasting plasma glucose [FPG] \geq 110 mg/dL and < 126 mg/dL) should be **counseled about prevention of** DM. Intensive lifestyle interventions to prevent diabetes include both regular aerobic exercise and a calorie-restricted diet to promote and maintain weight loss. [**R=A**]
- 6. Persons with diabetes should be assessed for contraindications to angiotensin converting enzyme inhibitor (ACEI) use. [R=A]
- 7. Start/adjust treatment with ACEIs. [R=A]
- 8. Prescribe aspirin therapy (75 to 325 mg/day) for all adult patients with diabetes and evidence of cardiovascular disease. [R=A]



GUIDELINE KEY ELEMENTS

Primary Prevention

- Consider screening all adults (age \geq 45) for impaired glucose tolerance.
- Consider **aerobic exercise and diet** to achieve weight loss and prevent the progression of impaired fasting glucose.

Secondary Prevention

- Achieve individualized **HbA**₁**c** target through diet, exercise, medication, and patient education to prevent micro- and macrovascular complications.
- Reduce and control **blood pressure** to improve quality and length of life, and prevent micro- and macrovascular complications.
- Control **cholesterol** to reduce risk of cardiovascular disease.

Tertiary Prevention

- Screen annually for kidney disease.
- Screen annually for retinopathy using a dilated **eye examination** or retinal photography for patients with ocular risk factors or who have had retinopathy detected on a prior examination.
- Screen annually for **lower extremity** complications and risk stratification.

Health Preventive Measures

- Consider **aspirin** therapy to reduce the risk of cardiovascular fatal events.
- Advise tobacco use cessation.
- Provide influenza vaccination in season.
- Provide **pneumonia vaccine**, if indicated.

Patient Education

• Empower patients to make informed decisions about their **self-care of diabetes**.

MODULE D - CORE

GENERAL

- 1. Children with diabetes should be referred to a pediatric diabetic team for consultative care.
- 2. All women of reproductive potential with pre-existing diabetes should be counseled to plan and prepare for each pregnancy.
- 3. All female patients of reproductive potential with diabetes should be counseled on the need for optimal glycemic control.
- 4. Diabetes mellitus (DM) management should be evaluated in the context of the patient's total health status.
- 5. Urgent or semi-urgent medical conditions, including severe hypo- or hyperglycemia, must be treated before long-term disease management principles are applied.
- 6. Determine and document if DM is type 1 or 2.

ASPIRIN THERAPY

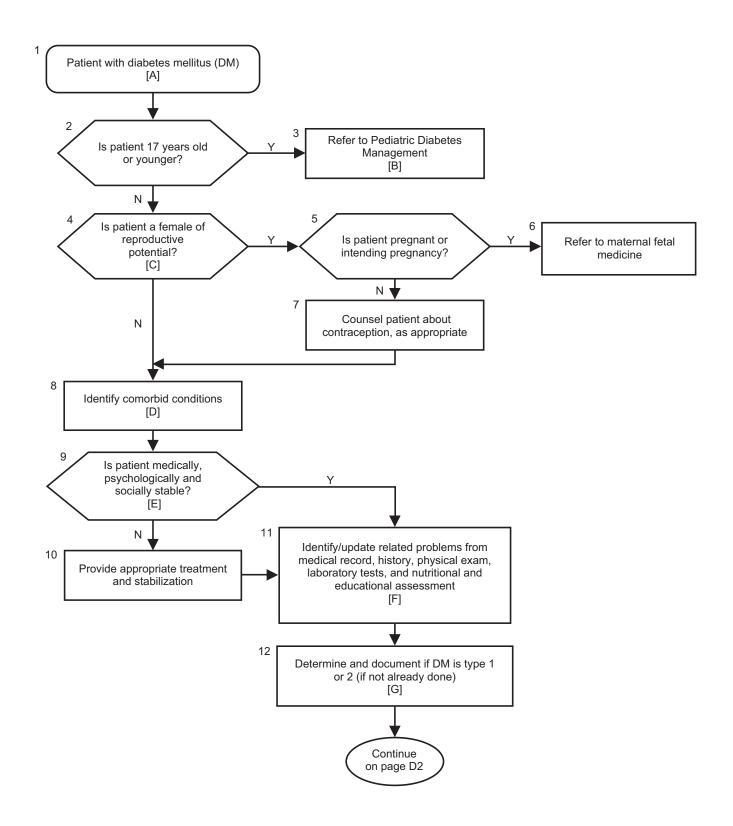
- 1. Prescribe aspirin therapy (75 325 mg/day) for all adult patients with DM and evidence of cardiovascular disease.
- 2. Consider beginning aspirin therapy (75 325 mg/day) for primary prevention in patients with diabetes age > 40 and one or more other cardiovascular risk factors.
- 3. Consider individual evaluation for aspirin therapy for patients between 30 and 40 years with DM, particularly those with other cardiovascular risk factors or with type 1 DM and long duration of disease.

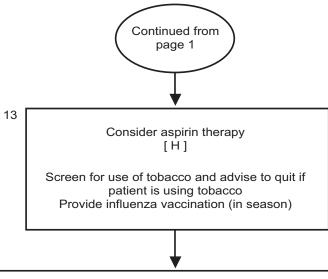
MANAGEMENT OF DIABETES

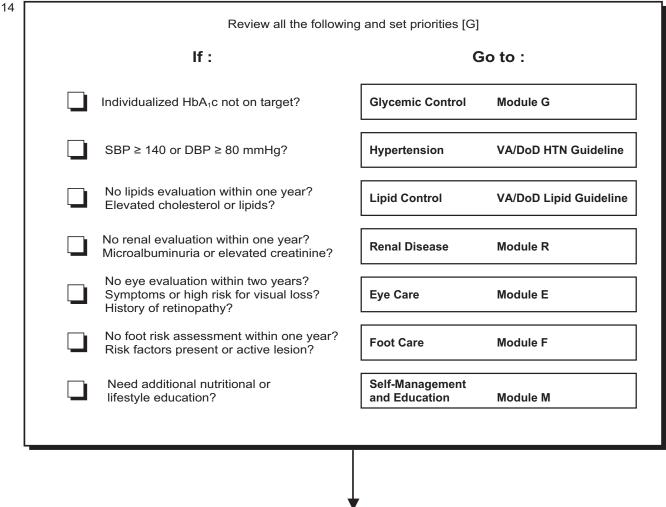
- 1. If the individualized HbA₁c is not at target, refer to **Module G Glycemic Control.**
- 2. If systolic blood pressure (SBP) ≥ 140 or diastolic blood pressure (DBP) is ≥ 80 mmHg, refer to the VA/DoD Clinical Practice Guideline for the Management of **Hypertension.** (Also see Annotation J.)
- 3. If a lipids evaluation was not done within one year or the patient has elevated cholesterol or lipids, refer to the VA/DoD Clinical Practice Guideline for the Management of **Dyslipidemia** (**Lipids**). (**Also see Annotation K.**)
- 4. If a kidney evaluation was not done within one year or the patient has micro-/macroalbuminuria or elevated creatinine, refer to **Module R Kidney Function**.
- 5. If an eye evaluation was not done within two years, the patient has symptoms, or a previous exam showed a high risk for visual loss or retinopathy, refer to **Module E Eye Care**.
- 6. If a foot-risk assessment was not done within one year or the patient has risk factors or an active lesion, refer to **Module F Foot Care**.
- 7. If the patient needs additional nutritional or lifestyle education, refer to **Module M Self-Management** and Education.
- 8. If the patient is a candidate for an **influenza vaccine**, administer it in season.
- 9. Administer **pneumonia vaccine** if indicated. (See VA/DoD Preventive Index Guideline.)
- 10. If the patient is using tobacco, refer to the VA/DoD Clinical Practice Guideline for the Management of **Tobacco Use Cessation**.

Management of Diabetes Mellitus Module D - Core Algorithm

D







Follow up as indicated

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TABLE D1: DIAGNOSIS OF DIABETES MELLITUS

Status	Tests	
	Fasting Plasma Glucose (FPG) (Preferred) ^{(a), (b)}	Casual Plasma Glucose
Diabetes Mellitus	≥ 126 mg/dL (7.0 mmol/L)	≥ 200 mg/dL (11.1 mmol/L) plus symptoms of diabetes (c)
Impaired Glucose Tolerance	≥110; < 126 mg/dL	_
Normal	< 110 mg/dL	_

⁽a) Fasting is defined as no caloric intake for at least 8 hours.

FPG is the preferred test for diagnosis, but either of the two listed is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these two tests should be used on a different day to confirm the diagnosis.

⁽c) "Casual" means any time of day without regard to time since the last meal; classic symptoms include polyuria, polydipsia, and unexplained weight loss.

TABLE D2. EVALUATION OF THE DIABETIC PATIENT

On a follow-up visit, the evaluation should focus on updating new information and/or changes to the patient record.

Evaluation Component	History – Patient/Family	Physical Examination	Laboratory
Glycemia	 Home glucose monitoring records Hyperglycemia Ketoacidosis Hypoglycemia Lifestyle Nutrition Current and past medications Also consider secondary etiologies: Cushing's disease Acromegaly Hemochromatosis Medications 	Weight Height Body mass index (BMI) BMI = Wt(kg)/(Ht[m])squared	 HbA₁c Fasting glucose
Foot	 Symptoms of neuropathy: Pain Paresthesia Symptoms of peripheral vascular disease Symptoms of systemic or local infection Previous episodes of foot complications: Foot deformity Skin breakdown Ulcers Amputations 	 Visual inspection including: Nails Web spaces Ulcers Calluses Deformities Palpation of pulses and determination of sensation (consider using a 5.07 monofilament) 	N/A
Eye	Changes in visionLaser treatmentGlaucomaDilated retinal exam by eye care provider within last year	Visual acuity, if changes in vision are reported	N/A
Kidney	Known history of diabetic disease Family history of hypertension and renal disease	• Edema	 Routine urinalysis Test for micro-albuminuria and serum creatinine level, if indicated
Hypertension	Previous diagnosis of hypertension Current and previous medications	Blood pressure	N/A

Evaluation Component	History – Patient/Family	Physical Examination	Laboratory
Coronary and Peripheral Arterial Disease/ Hyperlipidemia	Atherosclerotic disease: • Myocardial infarction (MI)/angina • Stroke • Transient ischemic attack (TIA) • Claudication • Surgical history of revascularization Atherosclerotic risks other than diabetes: • Smoking history • Family history • Previous diagnosis of hyperlipidemia; triglycerides Current and previous medications: • Aspirin • Estrogen therapy • Hypolipidemics	Cardiac examination: Heart Peripheral circulation including pulses and bruits Cutaneous or tendinous xanthomata	Electrocardiogram (EKG) Fasting lipid profile, if not done within the last year
Neurovascular	Sensory state of hands and feet	Interosseous muscle wasting Deep tendon reflexes	N/A
Self-Management Education	Knowledge, understanding, and self-described behaviors of : • Use of medication • Goals of treatment • Diet and self-management skills • What to do in case of complications	Observation: • Home glucose monitoring, if indicated • Foot self-examination	N/A
Other	Dental history and oral exam Dental and gingival health	Oral examination	N/A
	InfectionsInsulin injection sitesImmunizations: flu and pneumovax	N/A	N/A

TABLE D3. CLINICAL CLASSIFICATION OF DM

In a primary care setting, the patient's age at the time DM is diagnosed, plus the BMI and level of urinary ketones, are usually sufficient to classify the patient.

	Likely Type 1	Indeterminate	Likely Type 2
Age	< 30 years	30 – 40 years	> 40 years
ВМІ	< 25 BMI*	25 – 27	> 27
Urinary ketones	Moderate to large	Low to moderate	None to low

^{*}For Asian/Pacific Islanders the BMI threshold should be 23.

TABLE D4. LDL-C THRESHOLDS FOR INITIAL DYSLIPIDEMIA TREATMENT IN PATIENTS WITH DIABETES

The following table summarizes the thresholds and goals for dyslipidemia treatment.

	Baseline LDL-C [mg/dL]	
	≥100	≥130
Diabetes (with or without known CHD)	Diet/exercise Consider drug	Diet/exercise Initiate drug therapy

Adapted from NCEP (ATP III, 2001)

TABLE D5. HIGH TRIGLYCERIDE (TG) THERAPY (VA-HIT, 1999)

	Action	Remarks
TG 400 – 1000 mg/dL	Consider gemfibrozil if HDL-C < 40 mg/dL	For high TG, use direct LDL-C measurement or non-HDL-C as lipid disorder to guide therapy.

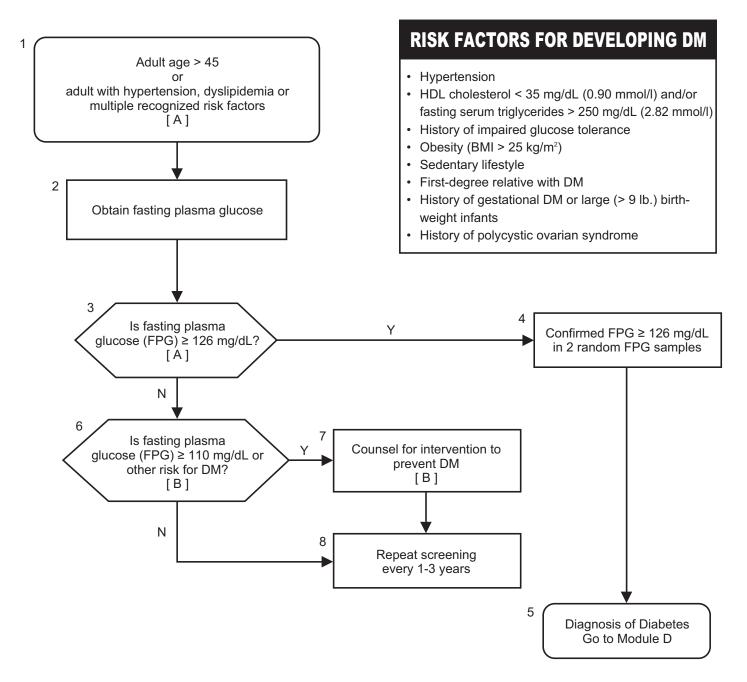
MODULE S – SCREENING FOR DIABETES

SCREENING

- 1. Screening for DM should be considered for adults age \geq 45 at 1- to 3-year intervals.
- 2. Screening should be considered in younger nonpregnant adults who have hypertension or dyslipidemia or multiple other recognized risk factors for DM. Risk factors include history of impaired glucose tolerance (IGT), body mass index (BMI) $> 25 \text{ kg/m}^2$, sedentary lifestyle, first-degree relative with DM, history of gestational diabetes mellitus (GDM) or large (> 9 lb) birth-weight infants, hypertension, high density lipoproteins-cholesterol (HDL-C) < 35 mg/dL (0.90 mmol/l) and/or fasting serum triglycerides > 250 mg/dL (2.82 mmol/l), history of polycystic ovarian syndrome, member of a high-risk ethnic population (e.g., African-American, Latino, Native American, Asian-American, and Pacific Islander), impaired fasting glucose (IFG) on previous testing, or other clinical conditions associated with insulin resistance.
- 3. Fasting plasma glucose (FPG) is the preferred screening test for DM and is also a component of diagnostic testing. DM is diagnosed if the value is ≥ 126 mg/dL on at least two occasions (see Module D, Annotation A). A normal FPG is < 110 mg/dL. An FPG ≥ 110 and < 126 mg/dL (7.0 mmol/l) is an indication for retesting, which should be done on a different day.
- 4. Although not recommended as a first-line screening test, casual non-fasting plasma glucose > 200 mg/dL (on at least two occasions) is sufficient to diagnose DM, and < 110 mg/dL is sufficient to exclude it. Random (non-fasting) plasma glucose in the range 111–199 mg/dL should be followed up with fasting plasma glucose.

PREVENTION

- Patients with IGT (i.e., FPG ≥ 110 mg/dL and < 126 mg/dL) should be counseled for intervention to prevent DM. Intensive lifestyle interventions to prevent DM include both regular aerobic exercise and a calorie-restricted diet to promote and maintain weight loss.
- 2. Patients with BMI > 25 are at high risk for DM and should achieve and sustain weight loss of 5 percent or more.
- 3. Modification of lifestyle may be beneficial for all patients and may be considered in patients with risk factors for DM (other than IGT).



Note:

Random non-fasting plasma glucose is not recommedned as first-line screening. However, non-fasting plasma glucose > 200 mg/dL (on at least two occasions) is sufficient to diagnose DM, and < 110 mg/dL is sufficient to exclude it. Random (non-fasting) plasma glucose in the range 111-199 mg/dL should be followed up with a fasting plasma glucose.

MODULE G – GLYCEMIC CONTROL

ASSESSMENT

- 1. Measure **HbA**₁**c** periodically–assess glycemic control over time.
- 2. Assess the postprandial plasma glucose (**PPG**) level for patients with:
 - Elevated HbA₁c (not at target) but a normal fasting plasma glucose level.
 - Frequent troublesome hypoglycemic symptoms during waking active hours.

Use the PPG level to modify the therapy.

- 3. Patients with recurrent or severe **hypoglycemia** should be evaluated for precipitating factors that may be easily corrected (e.g., missed meals, incorrect administration of insulin [dosage or timing], and exercise).
- 4. Patients with DM should be assessed for **knowledge**, **performance skills**, **and barriers** (e.g., psychosocial, personal, or financial) to full compliance.

GLYCEMIC CONTROL TARGET RANGE

- 1. Each patient's glycemic target range must be individualized, based on the provider's appraisal of the risk-benefit ratio for that individual, and the patient's medical, social, and psychological status. The risk of hypoglycemia should be specifically considered in recommending the target goal.
 - HbA₁c target should be kept < 9 percent for all patients to avoid symptoms of hyperglycemia.
 - For patients with very mild or no microvascular complications of DM and those free of major concurrent illnesses and with a reasonable life expectancy, the HbA₁c target should be < 7 percent.
 - For patients with advanced microvascular complications and/or major comorbid illness, or who have a shortened life expectancy (5–10 years), aggressive glucose lowering may not be warranted because of limited benefit in reducing the absolute risk of microvascular complications.
 - Individual treatment goals must be established with the patient based on the extent of the disease, comorbid conditions, and patient preferences.

TREATMENT OPTIONS

- 1. Patients with type 1 DM should receive insulin replacement therapy.
- 2. On at least a temporary basis, the use of intermediateor long-acting insulin for controlling fasting plasma glucose, alone or in addition to oral agents, should be considered for patients with type 2 DM in whom:
 - Oral agents have proven ineffective, intolerable, or are contraindicated.
 - Rapid restoration of euglycemia is desirable (e.g., patients with persistent symptoms of DM or with hyperglycemia in perioperative and/or critical care settings).
 - Pregnancy is desired or has already occurred.
 - HbA₁c is > 1.5 percent above target.
 - Relative insulin deficiency is suggested by weight loss and persistent, non-fasting ketosis.
- 3. Diet and exercise and lifestyle modification should be encouraged.
 - Institution of diet and exercise is usually the appropriate initial management in patients with new onset type 2 DM, depending upon the severity of the symptoms, psychosocial evaluation, and overall health status.
- 4. If treatment goals are not achieved with diet and exercise alone, drug monotherapy should be initiated.
 - Initial monotherapy with a sulfonylurea or biguanide (i.e., metformin) should be used as first-line drug therapy. Sulfonylurea can be considered for most patients with type 2 DM; however, for those who are significantly overweight (BMI > 25), initial monotherapy with a biguanide may be preferable.
 - Thiazolidinediones (TZDs) are NOT recommended as monotherapy for patients with type 2 DM, unless there is documented and unacceptable intolerance to metformin and available sulfonylurea agents.
 - Other oral agents, while less effective, are still appropriate first-line agents if the desired decrease in HbA₁c is proportionally less or if there are additional contraindications to the other first-line medications.

5. If the glycemic target level is not achieved with one oral agent alone, combination oral and/or insulin therapy is recommended.

Combination Oral Agent Therapy

- A biguanide (i.e., metformin) may be combined with a sulfonylurea.
- Alpha-glucosidase inhibitors may be used in conjunction with a sulfonylurea or sulfonylurea/biguanide combination in patients whose postprandial blood glucose is inadequately controlled, but whose fasting glucose is in the desired range on sulfonylurea or sulfonylurea/biguanide regimens.
- Addition of a TZD in failed monotherapy with a sulfonylurea should be considered only if the addition of metformin has failed and HbA₁c is within 1.5 percent of the target level. Addition of insulin to a sulfonylurea should be considered if a > 1.5 percent decrease in HbA₁c is desired.

Addition of Oral Agents to Insulin Therapy

- Addition of bedtime insulin therapy to an existing combination oral agent regimen may be a treatment option when the glycemic control target is not achieved by an all-oral regimen. Intermediate-acting insulin in a single bedtime dose may be used in conjunction with oral monotherapy with either sulfonylurea or biguanide, or in addition to combined sulfonylurea/biguanide therapy.
- Biguanide (i.e., metformin) or TZDs can be considered as an adjuvant therapy to insulin for the purpose of achieving glycemic target goals. Metformin is the preferred agent to add to an existing insulin regimen because of equal efficacy to glitazones and a known safety profile. TZDs are an alternative if metformin is contraindicated or a trial of metformin has failed to achieve the target HbA₁c. Addition of oral agents with existing insulin may be considered in the following circumstances:
 - Patient is on > 1 unit per kg of insulin in divided dosages, AND
 - Insulin dose has been actively adjusted in an attempt to improve glycemia, AND
 - HbA_1c is > 1 percent above the target, AND
 - There is documented adherence to medical nutrition therapy (MNT) or a referral to MNT.

Baseline and follow-up efficacy (at 6 months) are necessary for continuation of oral therapy. A referral to a diabetes care team for assistance with patient

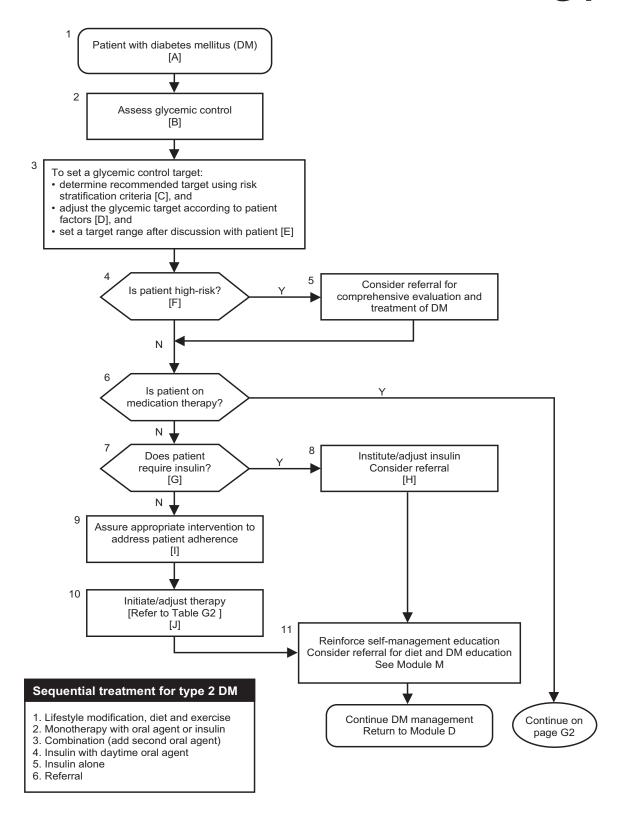
- management should be considered.
- In patients treated with large doses of insulin, addition of a TZD may reduce the insulin requirement and produce improved glycemia, with reduction of HbA₁c by 1 percent.
- Carefully selected individuals may benefit from three-drug oral hypoglycemic therapy. In general, these patients may benefit from referral to a diabetes care team.
- 6. Insulin therapy may also be used when given in multiple daily doses, if the glycemic control target has not been reached with oral therapy.
 - Insulin lispro or glargine is not recommended for routine use in the treatment of type 2 DM, as there is no evidence that it is inherently superior to more established insulin preparations in lowering HbA₁c levels.
 - Insulin glargine may be considered in the following settings:
 - In the insulin-treated patient with frequent, severe nocturnal hypoglycemia.
 - As a basal insulin for patients on multiple daily insulin injections.
 - In patients treated with insulin, regular insulin is recommended for most patients who require mealtime coverage.
 - Dietary counseling and individualized education should accompany initiation or change of mealtime insulin in response to hyperglycemia or hypoglycemia.
 - In patients treated with insulin, alternatives to regular insulin include aspart and lispro, which should be considered in the following settings:
 - Demonstrated requirement for pre-meal insulin coverage due to postprandial hyperglycemia AND concurrent frequent hypoglycemia
 - Patients using an insulin pump (Note: aspart is FDA-approved for use in an insulin pump; satisfactory outcomes have also been reported using lispro in pumps.)
- 7. Patients who fail to attain the target glycemic control goal despite ongoing care, education, and medication adjustment in the primary care setting may benefit from referral to a diabetes care team for comprehensive assessment and intensified management.

FOLLOW-UP

- 1. Patients should be scheduled for appropriate followup to evaluate response, tolerability to therapy, goal reassessment and management of acute and chronic problems.
 - The frequency of primary care provider visits for patients with DM who are meeting treatment goals and who have no unstable chronic complications should be individualized.
- When there is a sudden change in health status or when changes are made to the treatment regimen, follow-up within one month or sooner may be appropriate.
- 2. Treatment goals should be periodically reassessed based upon patient-specific factors, including changes in the patient's health status, adverse drug reactions, adherence to therapy, and preferences.

MANAGEMENT OF DIABETES MELLITUS Module G - Glycemic Control

G1



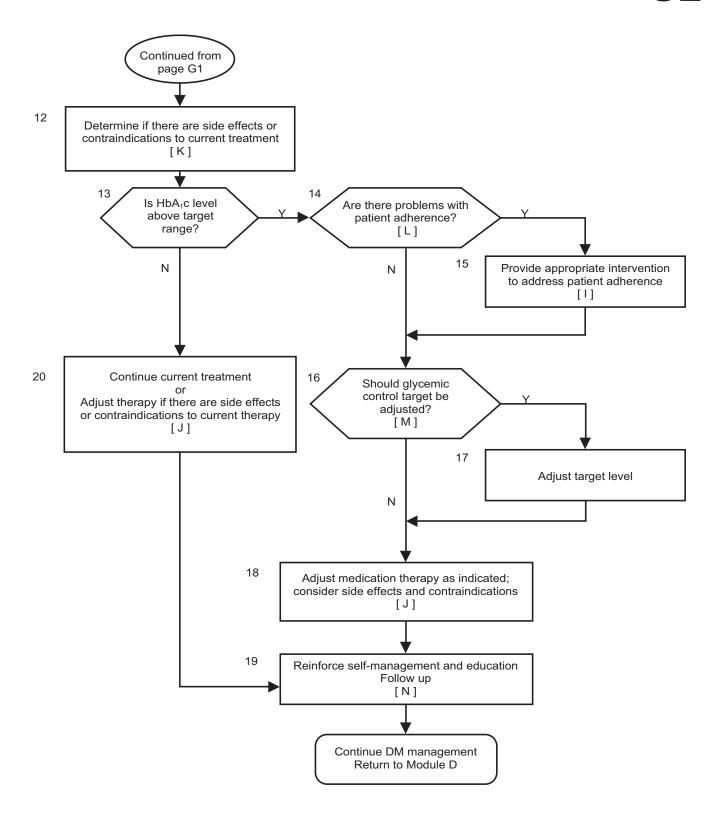


TABLE G1. DETERMINATION OF TARGET HBA₁C LEVEL

Use the following table as an overall perspective in determining individual glycemic control target based on consideration of microvascular complications and major comorbid illness.

Major Comorbidity ^(d)	Microvascular Complications		
or Physiologic Age	Absent or Mild (a)	Moderate ^(b)	Advanced ^(c)
Absent > 15 years life expectancy	7% (< 1% above upper normal range)	< 8% (< 2% above upper normal range)	< 9% (< 3% above upper normal range)
Present ^(e) 5 – 15 years life expectancy	< 8 % (< 2% above upper normal range)	< 8% (< 2% above upper normal range)	< 9% (< 3% above upper normal range)
Marked [®] < 5 years life expectancy	< 9% (< 3% above upper normal range)	< 9% (< 3% above upper normal range)	< 9% (< 3% above upper normal range)

⁽a) Mild microvascular disease is defined by early background retinopathy, and/or microalbuminuria, and/or mild neuropathy.

TABLE G2: SEQUENTIAL TREATMENT FOR TYPE 2 DM

The concept of sequential treatment is commonly employed in clinical management of chronic diseases. The sequential steps for glycemic control therapy are summarized in this table.

	Therapy	Drugs	Expected reduction in HbA₁c*
1	Lifestyle modification, diet and exercise	None	_
2	Lifestyle modification, diet and exercise <i>and</i> Monotherapy with oral agent or insulin	Sulfonylurea or biguanide	1 – 2%
3	Lifestyle modification, diet and exercise and Combination (add a second oral agent)	Sulfonylurea + biguanide Sulfonylurea/biguanide + alpha-glucosidase inhibitor Sulfonylurea/biguanide + thiazolidenedione Biguanide + repaglinide/ nateglinide	1 – 2% 0.5 – 1% 0.7 – 1.75% 0.1 – 0.3%
4	Insulin with oral agent.	Biguanide + insulin Thiazolidenedione + insulin Sulfonylurea + insulin	0.2 – 2.6%
5	Insulin	Insulin alone	2%
6	Referral	None	_

^{*}Over a 2- to 3-month period of follow-up

Moderate microvascular disease is defined by pre-proliferative (without severe hemorrhage, intra-retinal microvascular anomalies [IRMA], or venous bleeding) retinopathy or persistent, fixed proteinuria (macroalbuminuria) and/or demonstrable peripheral neuropathy (sensory loss).

Advanced microvascular disease is defined by severe non-proliferative (with severe hemorrhage, IRMA, or venous bleeding) or proliferative retinopathy and/or renal insufficiency (serum creatinine level > 2.0 mg/dL) and/or insensate extremities or autonomic neuropathy (e.g., gastroparesis, impaired sweating, or orthostatic hypotension).

Major comorbidity includes, but is not limited to, any or several of the following conditions: cardiovascular disease, chronic obstructive pulmonary disease, chronic liver disease, stroke, and malignancy.

⁽e) Moderate degree of major comorbid condition.

⁽f) Severe degree or end-stage major comorbid condition.

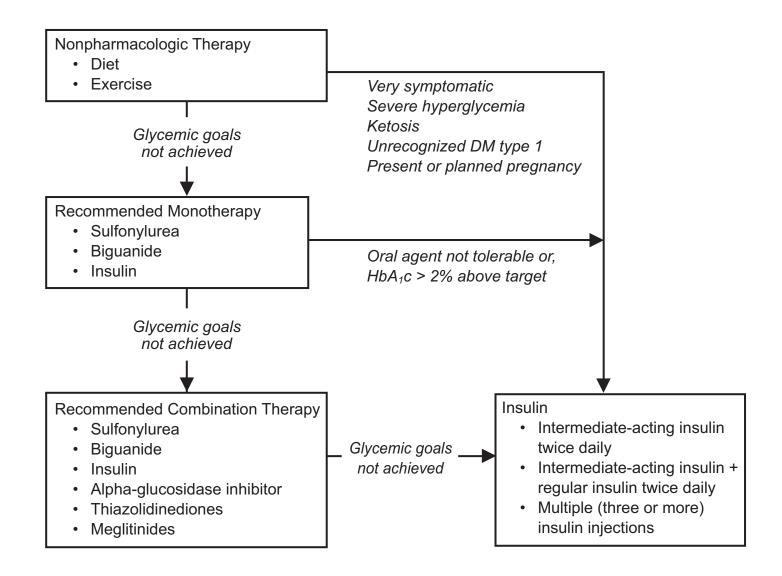


TABLE G3: ESTIMATE OF HBA₁C

Assuming that the mean **Self-Managed Blood Glucose** (SMBG) or point of care or laboratory glucose measurements are accurate, multiple readings at various time points can be averaged to obtain approximate HbA₁c levels by using the equation shown in Table G6, from the Diabetic Control and Complication Trial (DCCT) database.

Mean Blood Glucose	Estimated HbA₁c
120 mg/dL glucose	6% HbA₁c
150 mg/dL glucose	7% HbA₁c
180 mg/dL glucose	8% HbA₁c
Every 30 mg/dL increase	1% increase

TABLE G4. ORAL PHARMACOLOGIC AGENTS

Sulfonylureas

- Efficacy ($\downarrow HbA_1c$) = 1.0 2.0 %.
- First-generation sulfonylureas are no longer commonly used.
- No difference in long-term efficacy or failure rate has been demonstrated among the sulfonylureas.
- The preferred agents have shorter half-lives and inactive metabolites.
- First-generation sulfonylureas are 100% renally eliminated. Chlorpropamide and tolazamide have active metabolites.
- Glipizide, glyburide, and glimepiride are renally eliminated by 80 85%, 50%, and 60%, respectively. All but glipizide have active metabolites.
- · Inexpensive

Agents	Dose	Contraindications	Adverse Events
Chlorpropamide	100 – 500 mg qd	Hypersensitivity	Hypoglycemia
Tolazamide	1000 mg given qd or divided into 2 doses	Pregnancy	 Hypersensitivity (rash, etc.)
Tolbutamide	250 – 2000 mg divided into 2 – 3 doses		Weight gain
2nd generation			
Glimepiride	1 – 4 mg qd		
Glipizide* Glipizide XL*	2.5 – 40 mg given qd or divided into 2 doses taken 30 minutes before a meal Doses > 15 mg should be divided into 2 doses. 5 – 10 mg qd		
Glyburide* Micronized glyburide*	1.25 – 20 mg given qd or divided into 2 doses 0.75 – 12 mg given qd or divided into 2 doses; doses > 6 mg may provide a better response when divided. If the response to a single daily dose of glybride or glipizide does not achieve treatment goals, dividing the dose may be effective.		

^{*} In general, the hypoglycemic effects of glyburide and glipizide tend to plateau at 10 mg and 20 mg, respectively.

Biguanide

- Efficacy (↓HbA₁c) 1.0 2.0%.
- The major blood glucose–lowering effect is through decreasing hepatic glucose production with some decrease in peripheral insulin resistance.
- May restore ovulation in premenopausal anovulatory females.
- Monitor renal function prior to drug initiation and at least annually thereafter.
- Inexpensive when using generic

Agents	Dose	Contraindications	Adverse Events
Metformin	Starting dosage is either 500 mg bid or 850 mg q am: If on 500 mg bid, dosage increase may be made by 500-mg increments weekly up to 1000 mg bid If on 850 mg q am, dosage increase of 850 mg may be made every other week (given as 850 mg bid) The usual maintenance dose is 850 mg bid with meals. Maximum dose: 2550 mg/day (850 mg tid); the dose response curve usually plateaus after 2000 mg/day. Take with food to avoid possible GI symptoms.	 Contraindications Renal dysfunction (SCr > 1.5 mg/dL for males or > 1.4 mg/dL in females) Chronic heart failure requiring pharmacologic management Acute or chronic metabolic acidosis Temporarily discontinue metformin use at the time of or prior to intravascular iodinated radiocontrast studies and withhold for 48 hours after the procedure. Reinstitute only after renal function has been reevaluated and found to be normal. Not Recommended ≥ 80 years of age unless normal creatinine clearance, and the dose should not be escalated to the maximum in elderly patients due to increased susceptibility to lactic acidosis Hepatic disease or excessive ethanol 	Potential for lactic acidosis when used in patients for whom the drug is contraindicated Transient dose-related GI symptoms (diarrhea, nausea, vomiting, bloating, flatulence, anorexia) Decrease in vitamin B12 levels
Metformin extended release	Begin with 500 mg daily with the evening meal. Dose may be increased by 500 mg per week to a maximum of 2000 mg qd. If glycemic control is not achieved, consider dividing into 2 doses.	 intake Withhold metformin in the presence of any condition associated with hypoxemia, dehydration or sepsis. 	

Alpha-glucosidase inhibitors

- Efficacy (↓HbA₁c) 0.4 1.0%
- Delays the digestion of carbohydrates, thereby decreasing postprandial hyperglycemia.
- · Allows for flexible meal dosing.
- Moderately expensive.

Agents	Dose	Contraindications	Adverse Events
Acarbose Miglitol	For acarbose or miglitol begin with 25 mg tid or initiate gradually: 25 mg qd x 1 – 2 weeks followed by 25 mg bid for 1 – 2 weeks followed by 25 mg tid. Once a 25 mg tid dosing regimen is reached, further increases may be made at 4 – 8 week intervals. The usual maintenance dose is 50 mg tid. Maximum dose for acarbose is 100 mg tid (50 mg tid if weight < 60 kg) and 100 mg tid for miglitol. Dose is to be taken with the first bite of each main meal. If the patient misses or adds a meal, he/she should omit or add the dose.	Contraindications Intestinal complications (inflammatory bowel disease, colonic ulceration, intestinal obstructions, digestion or absorption disorders) Acarbose is contraindicated in patients with cirrhosis. Miglitol pharmacokinetics are not altered in cirrhosis and may be used. Not Recommended SCr > 2.0 mg/dL	 Transient dose-related GI symptoms (diarrhea, abdominal pain, flatulence) which can limit compliance with therapy Acarbose, especially at doses > 50 mg tid, may cause serum AST/ALT elevation; monitor serum levels every 3 months during the first year of treatment.

Thiazolidinediones

- Efficacy (↓HbA₁c) 1.0 1.5%.
- Enhances insulin sensitivity in skeletal muscle, hepatic, and adipose tissue without directly stimulating insulin secretion from the pancreas. Also has a small effect on inhibiting hepatic glucose.
- Liver function tests and bilirubin should be tested every 2 months for 1 year, then periodically thereafter. If ALT is > 3x upper limit of normal, recheck another level as soon as possible. If ALT remains > 3x the upper limit, discontinue use.
- May restore ovulation in premenopausal anovulatory females.
- · Very expensive.

Agents	Dose	Contraindications	Adverse Events
Agents Rosiglitazone Pioglitazone	Dose 4 – 8 mg/day, given qd or divided into 2 doses 15 – 45 mg administered qd May be given without regard to meals, no dosage adjustment required for renal insufficiency, and the current sulfonylurea, metformin, or insulin dose should be continued when adding rosiglitazone or pioglitazone. When using with insulin, if plasma glucose levels decrease to less than 100-120 mg/dL, the dose of insulin	Not Recommended New York Heart Association Class III and IV Do not initiate in patients with ALT > 2.5x the upper limit of normal.	Adverse Events Edema Weight gain Decrease Hgb/HCT Hepatotoxicity (rare)
	should be decreased by 10-25%. Continue to monitor the patient for further adjustments.		
	Slow onset of action.		

Meglitinides

- Efficacy (↓HbA₁c) 0.6 1.9%
- Like sulfonylureas (SFU), it stimulates pancreatic secretion of insulin. It has a faster onset and shorter duration of action than SFUs, therefore postprandial glucose is affected to a greater extent than fasting blood glucose.
- Allows for flexible meal dosing
- Do not use in patients who have failed sulfonylurea therapy.
- Expensive

Agents	Dose	Contraindications	Adverse Events
	Take 1 – 30 minutes before a meal. If the patient misses or adds a meal, he/she should omit or add the dose.	Use With Caution	HypoglycemiaWeight gain
Repaglinide	Repaglinide: Starting dose is 0.5 mg in patients with $HbA_1c < 8\%$. If the HbA_1c is $\geq 8\%$, a dose of 1 or 2 mg may be initiated. Maximum dose is 4 mg per meal.	RepaglinideHepatic impairmentSevere renal impairment	
Nateglinide	Nateglinide: 120 mg before each meal	Nateglinide Moderate-severe hepatic impairment	

TABLE G5: COMPARISON OF INSULIN PREPARATIONS^{a, b}

Insulin types and species have different pharmacological properties and should not be changed inadvertently.

Insulin	Onset (hours)	Peak (hours)	Duration (hours)	Compatible Mixed With	Appearance
		RAPID-ACTING	i		
Regular (Novolin R®, Humulin R®)	0.5 – 1	2 – 5	6 – 10	NPH, lente, ultralente	Clear
Lispro (Humalog®)	0.25 – 0.5	0.5 – 2.5	3 – 6.5	Human NPH, Human ultralente ^{c, d}	Clear
Aspart (Novolog®)	0.17 – 0.33	1 – 3	3 – 5	Human NPH ^{c, e}	Clear
	INTE	RMEDIATE-AC	TING		
NPH (Novolin N®, Humulin N®)	1 – 1.5	4 – 12	16 – 24	Regular	Cloudy
Lente (Novolin L®, Humulin L®)	1 – 2.5	7 – 15	16 – 24	Regular	Cloudy
LONG-ACTING					
Ultralente (Humulin U®)	4 – 6	8 – 20	24 – 28	Regular	Cloudy
Insulin glargine (Lantus®)	1.1	2 – 20	Up to 24	Not to be mixed with other insulins	Clear
PRE-MIXED PRODUCTS					
70%NPH/30% Regular (Novolin 70/30, Humulin70/30) 50%NPH/50% regular (Humulin 50/50)			Not to be mixed with other insulins	Cloudy	
75% intermediate/25% lispro (Humalog mix 75/25)			Not to be mixed with other insulins	Cloudy	

NPH= Neutral Protamine Hagedorn

⁽a) Adapted from AHFS Drug Information, American Society of Health-System Pharmacists, Inc., 2002

⁽b) The time course of action is intended as a general guide as many factors may influence these parameters (e.g., type of preparation, dose, site of administration, and patient-related variables).

⁽c) The effects of mixing insulin lispro or insulin aspart with insulins of animal source have not been studied. The only animal-source insulin remaining on the market is purified pork as regular, NPH, and lente.

⁽d) The effects of mixing insulin lispro with insulins produced by manufacturers other than Eli Lilly have not been studied.

⁽e) The effects of mixing insulin aspart with insulins produced by manufacturers other than Novo Nordisk have not been studied.

Table G6: Insulin Regimen Examples		
Bedtime dosing of NPH or lente insulin in addition to an oral agent	 Begin with 10 – 15 units at bedtime (a dose equal to the morning glucose/18^[a]). Verify that the pre-dinner glucose remains in control. 	
Split mixed regimen with NPH/regular (b)	 Inject 2/3 of the total insulin requirement in the morning, with a NPH/regular ratio of 70:30. Inject 1/3 of the total insulin requirement in the evening, with a NPH/regular ratio of 50:50^(c). 	
Once-daily morning NPH insulin	 Good for elderly or non-compliant patients Inject 30 – 60 minutes before breakfast Usual dosage < 40 units/day 	

⁽a) Adapted from Edelman et al., 1995.

Table G7: General Guidelines for Insulin Adjustment in Patients with Type 2 DM on Split Regimens

- If the morning fasting blood sugar is off target, adjust the evening NPH or switch evening NPH to bedtime.
- If the evening serum glucose is off target, adjust the morning NPH.
- If the evening glucose continues to be off target, have the patient check the pre-lunch glucose.
- · If the pre-lunch glucose is off target, adjust the morning regular insulin.
- If the bedtime glucose is off target, adjust the evening regular insulin.

⁽b) Always counsel patients to mix regular insulin in syringe first, followed by NPH; mixtures of regular and lente insulins should be injected immediately.

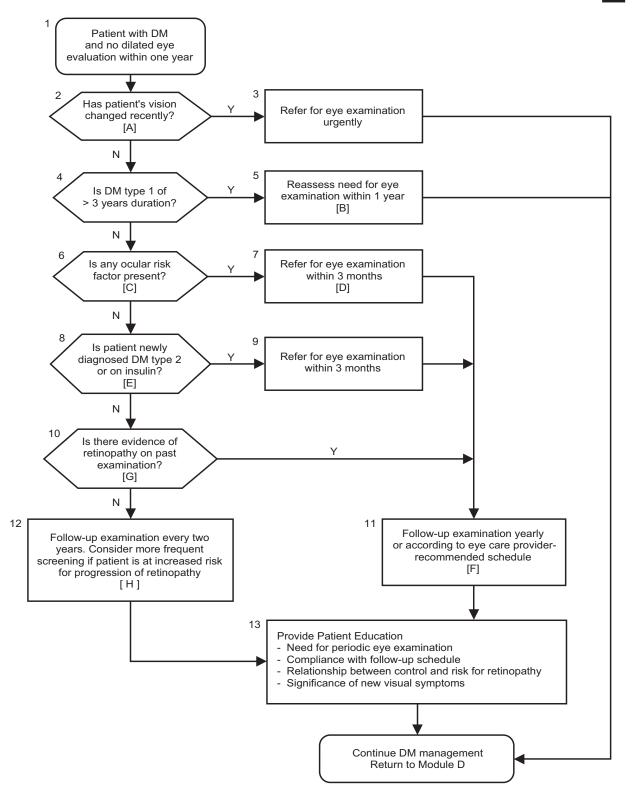
Inject regular insulin 30–60 minutes before a meal; lispro insulin should be injected within 15 minutes before a meal; mixtures of lispro and Humulin N or Humulin U should be administered immediately. Manufacturer specific storage guidelines should be followed.

⁽c) These are a few examples; optimal regimen depends on the individual patient.

MODULE E – EYE CARE

- 1. Retinopathy screening should be performed by a qualified professional using a dilated eye examination or a retinal image technique with proven accuracy, and interpreted by a trained reader or experienced eye care provider.
- 2. Routine retinopathy screening should be initiated for patients with type 1 DM within 3 years of the diagnosis and for patients with type 2 DM within 3 months of the diagnosis, at most. Patients with visual symptoms should be urgently referred.
- 3. Patients who have had no retinopathy on all previous examinations should be screened for retinopathy at least every other year (biennial screening).
- 4. More frequent screening should be considered in patients with clinical findings associated with an increased rate of progression or prevalence of retinopathy. These clinical findings include uncontrolled hypertension, chronic severe hyperglycemia,

- recent initiation or intensification of insulin therapy, or other known microvascular disease (e.g., albuminuria or neuropathy).
- 5. Patients who have ocular risk factors, are on insulin, or who have had retinopathy detected on a previous examination should have a yearly fundus examination. The eye care provider should determine the optimal screening intervals based on the patient's severity of retinopathy and risk factors associated with retinopathy progression.
- 6. Retinal imaging techniques cannot substitute for a comprehensive eye exam for other eye problems, when indicated. Periodic comprehensive eye examinations by a trained eye specialist should be scheduled by the primary care provider or eye care specialist based on the individual patient's risk factors for ocular disease, other than diabetic retinopathy.



MODULE F – FOOT CARE

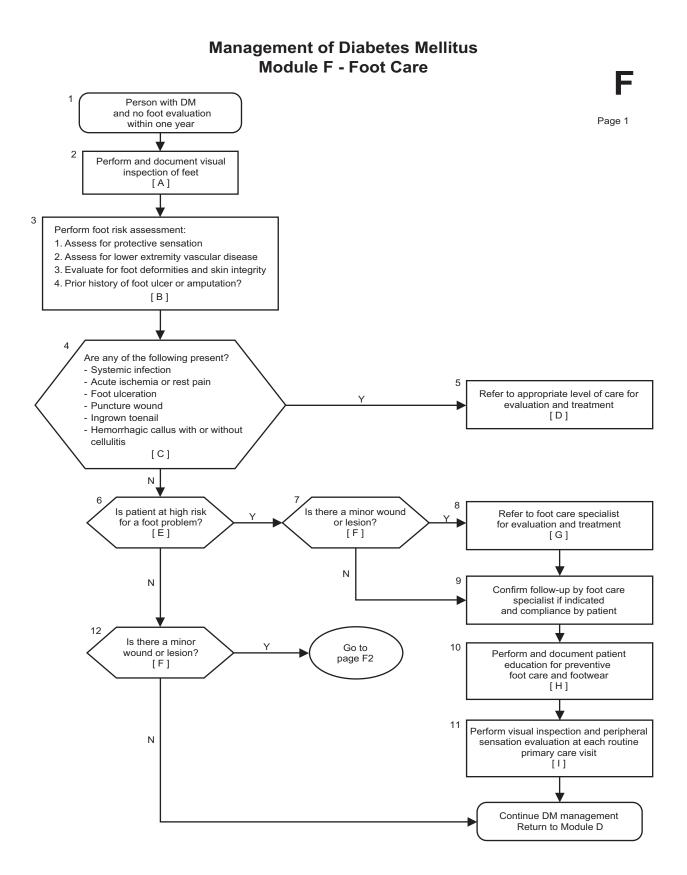
The goal of Module F – Foot Care is to identify patients who are at high risk for the development of foot ulcers and lower extremity amputations (LEA). Patients are identified through a foot risk assessment that stratifies them into either high risk or low risk for lower extremity (LE) complications. Once the patient is identified as high risk, he/she is referred to a foot care specialist for a more intensive follow-up plan that includes patient education, appropriate footwear, and other specialty referrals, as needed.

SCREENING AND ASSESSMENT

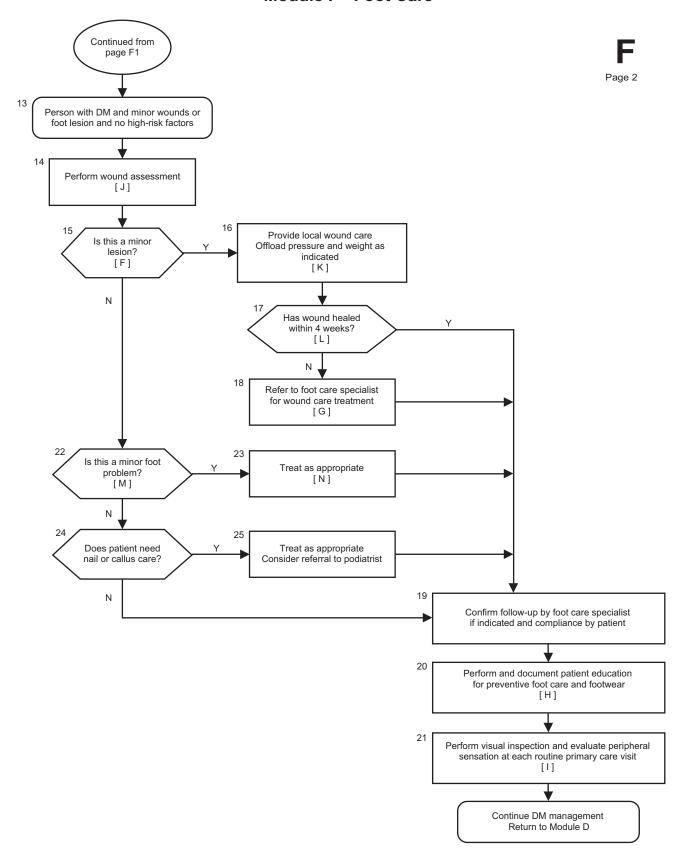
- 1. Visual inspection should be performed in high-risk patients at each routine primary care visit. Inspection includes screening for breaks in the skin, erythema, trauma, pallor on elevation, dependent rubor, changes in foot size/shape, nail deformities, extensive callus, tinea pedis, and pitting edema.
- 2. A foot risk assessment should be performed and documented annually to evaluate for skin breakdown, LE arterial disease, and foot deformity; assess protective sensation; determine prior history of ulcers or amputations; and evaluate footwear.
 - High-risk patients are defined as having at least one of the following characteristics:
 - Lack of sensation to Semmes-Weinstein 5.07 monofilament at one or more noncallused plantar sites
 - Evidence of LE arterial disease (absence of both dorsalis pedis and tibialis posterior pulses, dependent rubor with pallor on elevation, history of rest pain or claudication, and prior history of LE bypass surgery)
 - Foot deformities (specifically hammer toes, claw toe, Charcot's arthropathy, bunions, and metatarsal head deformities)
 - History of foot ulcer or non-traumatic LEA

TREATMENT/REFERRAL

- 1. Patients with life-threatening conditions should be referred to the appropriate level of care for evaluation and treatment.
- 2. High-risk patients or those with limb-threatening conditions (e.g., systemic infection, acute ischemia/rest pain, foot ulceration, puncture wound, ingrown toenail, and hemorragic callus with or without cellulites) should be referred to a foot care specialist for a more intensive treatment program of in-depth patient education concerning foot care practices, hygiene, and footwear.
- 3. Patients with circulatory symptoms that limit their lifestyle should be referred to a vascular specialist to determine the appropriateness of surgical intervention on a patient-specific basis. Vascular procedures should be justified based on outcomes of vascular interventions.
- 4. Patients with minor foot wounds or lesions should be referred to a foot care specialist (i.e., podiatrist, vascular surgeon, orthopedic surgeon, and other healthcare providers) with demonstrated training, competence, and licensure in foot care for evaluation and treatment.
- 5. Patients with uncomplicated minor lesions (e.g., onychomycosis, painful corns, dry skin, athlete's foot, minor calluses, uncomplicated nail trimming and improper foot hygiene) may be provided with local wound care and offload pressure, as indicated, with follow-up on a specified schedule.
- 6. Footwear prescriptions should be determined based upon the individual structural and clinical findings. Patients and families should be educated on preventive foot care and footwear including daily foot inspection and preventive care; skin, nail, and callus care; what to report and whom to call regarding any foot injury or abnormality; and footwear.



Management of Diabetes Mellitus Module F - Foot Care



MODULE R – KIDNEY FUNCTION

SCREENING

- 1. Patients with type 1 DM should be screened for kidney disease after puberty and at a minimum of every five years. Patients with type 2 DM should be screened for kidney disease at the time of DM diagnosis, since the onset of type 2 DM occurs on average 10 years before a clinical diagnosis is made.
- 2. Patients with DM who have a probable life expectancy of > 5 years should be screened for elevated urinary albumin or protein excretion using the cut-points adopted (Table R1) from the American Diabetes Association.
- 3. Patients with DM should be monitored annually for kidney function (estimated glomerular filtration rate [eGFR]), and protein-to-creatinine ratio.
- 4. The preferred method for nephropathy screening is a random spot urine sample to measure the albumin-to-creatinine ratio. A 24-hour urine collection for protein and creatinine may also be used, but is more cumbersome for patients and prone to collection errors.
 - Urine "strips" are not recommended for screening, because they do not take into account possible errors resulting from alterations in urine concentration.
 - Because of variability in urinary albumin excretion, two of three specimens collected within a 3- to 6month period should be abnormal before diagnosing microalbuminuria.
 - A urine albumin/creatinine test with results ≥ 30 µg/mg in a random specimen should be repeated to ensure that the level was not transiently elevated (by heavy exercise, urinary tract infection, acute febrile illness, or heart failure).

ASSESSMENT AND DIAGNOSIS

- 1. Serum creatinine level should be used to estimate the GFR to identify patients at risk and develop appropriate management plans.
- 2. Persons with DM and macroalbuminuria (i.e., urine albumin/creatinine ratio ≥300 µg/mg or 24-hour urine protein ≥300 mg/dL) should be assessed for kidney function as these levels of albuminuria indicate established to advanced diabetic renal disease.
 - Document the course of the albuminuria. It would be unusual to go from having normal urine to macroalbuminuria in less than one year in diabetic kidney disease.
 - Document that blood pressure has been rising. As diabetic kidney disease progresses from micro- to macroalbuminuria, the blood pressure usually rises.
 - Document the presence of other diabetic complications, such as retinopathy. All patients with DM with macroalbuminuria should undergo eye exams to confirm the diagnosis of retinopathy (findings include microaneurysm, flame hemorrhage, and soft/hard exudates) (see Module E Eye Care) because > 90 percent of patients with macroalbuminuria from DM will also have at least mild retinopathy.
 - If the course has been atypical (i.e., rapidly progressive or no evidence of retinopathy), refer or consult with nephrology for further work-up.
 - Consider alternative explanations for reduced kidney function including pre-renal, renal, and postrenal causes.
 - Obtain renal ultrasound in all patients with reduced kidney function except those whose reduced kidney function is easily resolved.
 - Consider obtaining other tests and referral to specialists in nephrology or urology as indicated.

TREATMENT

- Primary care providers should consult with or refer to a nephrologist when a patient has macroalbuminuria with normal creatinine but other features inconsistent with the sole diagnosis of diabetic nephropathy. These atypical features include absence of diabetic retinopathy on dilated eye exam, rapidly progressive course, short duration of DM, small kidneys on ultrasound, red blood cell casts in the urine, and/or lack of increase in blood pressure concurrent with increasing albuminuria.
- 2. Patients with DM with reduced kidney function may have electrolyte disturbances, anemia, or bone disease. Also, these patients' kidney failure may progress and they may need dialysis or evaluation for renal transplantation. For these reasons, an initial evaluation by nephrology for confirmation of diagnosis, optimal management of kidney disease, and appropriate timing of dialysis access is recommended for patients with chronic kidney disease or for acute kidney disease that does not rapidly resolve (see the VA/DoD Clinical Practice Guideline on Pre-ESRD).
- 3. Persons with DM should be assessed for contraindications to angiotensin converting enzyme inhibitor (ACEI) use.
- 4. Start/adjust treatment with ACEIs.

- 5. Change ACEI to angiotensin receptor blocker (ARB) if patient has an ACEI-induced cough. Angioedema risk may be lower with ARB vs. ACEI, but providers should use great caution if ARB is prescribed to a patient with a history of angioedema associated with ACEI use.
- 6. ACEI and ARB may cause similar rates of hyperkalemia and abrupt reduction of kidney function.
- 7. If the patient's macroalbuminuria is not improving, or DM and/or blood pressure is not controlled, consider a change in treatment.
- 8. Reevaluate the current treatment regimen (i.e., ACEIs, blood pressure control, and glycemic control) for patients with DM with progressing kidney disease.
- 9. Consider counseling patients with DM with macroal-buminuria (diabetic nephropathy) to reduce daily dietary protein allowance to 0.8 g/kg/day (~10 percent of calories).
- 10. If albuminuria is progressing or the estimated GFR continues to decline, consider increasing the ACEI to the maximum recommended dose, while reinforcing glycemic control and a low-protein diet.
- 11. Patients with DM on ACEIs should have a spot urine for albumin/creatinine ratio at 6 months from initiation of ACEI.

Table R2: Factors that Transiently Interfere with Urinary Screening for Albuminuria		
Increases in Albuminuria	Decreases in Albuminuria	
Blood in urine	ACEI/ARB	
Chronic heart failure	Malnutrition	
Exercise	NSAID	
Excessive protein intake		
Fever		
Uncontrolled diabetes		
Uncontrolled hypertension		
Urinary tract infection		
Vaginal fluid contamination of specimen		
Nonsteroidal anti-inflammatory drugs (NSAID)		

Table R3. Definition of Chronic Kidney Disease Criteria

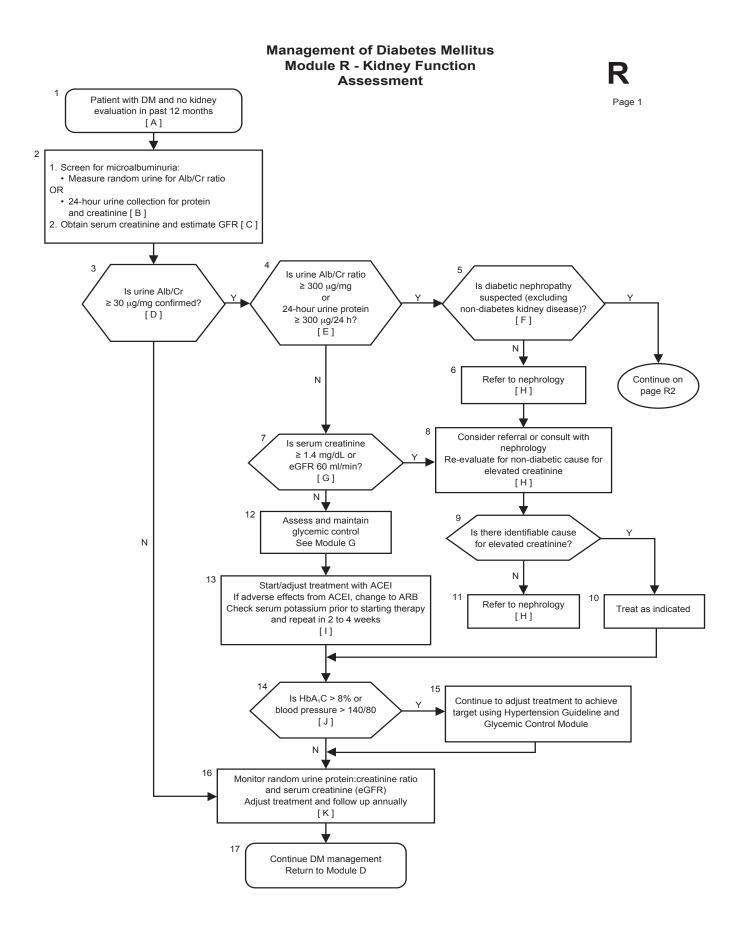
Chronic Kidney Disease Criteria

- 1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*:
 - · Pathological abnormalities; OR
- Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
- 2. GFR < 60mL/min/1.73m² for ≥ 3 months, with or without kidney damage

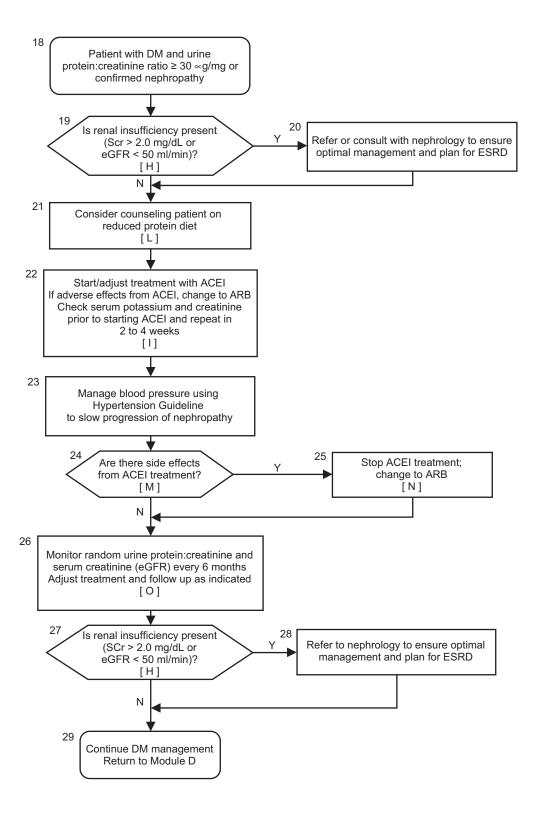
Table R4. Chronic Kidney Disease (CKD): A Clinical Action Plan				
Stage	Description	GFR (mL/min/1.73m²)	Action*	
	At increased risk	≥ 90 (with CKD risk factors)	Screening, CKD risk reduction	
1	Kidney damage with Normal or ↑ GFR	≥ 90	Diagnosis and treatment Treatment of comorbid conditions Slowing progression Cardiovascular disease risk reduction	
2	Kidney damage with Mild ↓ GFR	60 – 89	Estimating progression	
3	Moderate	30 – 59	Evaluating and treating complications	
4	Severe ↓ GFR	15 – 29	Preparation for kidney replacement therapy	
5	Kidney failure	< 15 (or dialysis)	Replacement (if uremia present)	

Unshaded area identifies patients who have CKD; shaded area designates individuals who are at increased risk for developing CKD. Chronic kidney disease is defined as either kidney damage or GFR < 60 mL/min/1.73 m² for ≥ 3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

^{*}Includes actions from preceding stages.



Management of Diabetes Mellitus Module R - Kidney Function - Treatment



MODULE M – SELF-MANAGEMENT AND EDUCATION

Diabetes self-management education (DSME) is considered necessary by most healthcare organizations to assist persons with DM in their day-to-day self-management and with making informed self-care choices. DSME includes providing the patient with behavioral strategies to help him/her establish and maintain a healthy lifestyle. Comprehensive education programs should address the patient's fluctuating diabetes clinical state over a lifetime and provide clinically relevant knowledge and skills to facilitate implementation of ever-changing treatment plans.

- 1. Education in core competencies, also known as "survival skills," should be provided to all patients newly diagnosed with DM. Core competency education includes: response to acute complications (hyperglycemia and hypoglycemia); how and when to take medication(s); self-monitoring of blood glucose, basic diet guidelines; sick-day management; and guidance on when and how to seek further treatment or medical advice.
- 2. Comprehensive education on self-management and diet should be provided to all patients newly diagnosed with DM. Education should be individualized and tailored to the patient's needs. Education can be provided through an in-house comprehensive diet consultation for medical nutrition therapy (MNT) or a comprehensive DSME program recognized by the American Diabetes Association; if neither of these options is available, comprehensive DSME should be provided at the provider's facility.
- 3. Upon completion of the initial DSME/MNT education, behavioral goals should be set and a follow-up visit schedule determined by the provider and patient.

- 4. Information sources (e.g., books, pamphlets and web sites) and points of contact for organizations and other relevant resources should be provided to all patients.
- 5. Assessment of the following factors should be completed to determine the extent of the patient's educational and skills deficit and his/her ability for self-management: knowledge of the diabetes disease process, treatment goals, management skills, cultural influences, health beliefs/behavior, attitudes, and socioeconomic factors and barriers.
- 6. At follow-up, the patient's understanding of, and knowledge about, DM should be reviewed. The provider should consider referring the patient to case management or other specialized care if the patient exhibits poor glycemic control, has high-risk factors, or fails to demonstrate good knowledge of self-care. The provider should coordinate the patient's care with caregivers to whom the patient has been referred and obtain updates on the patient's condition and needs.
- 7. The provider should always be ready to respond to the patient's *ad hoc* inquiries about new treatments, problems, or concerns.
- 8. As the patient's DM control and status improve or decline, the provider should readjust the follow-up schedule for less or more frequent visits. Continuing education may be necessary, based on the patient's needs.

Management of Diabetes Mellitus Module M - Self-Management and Education



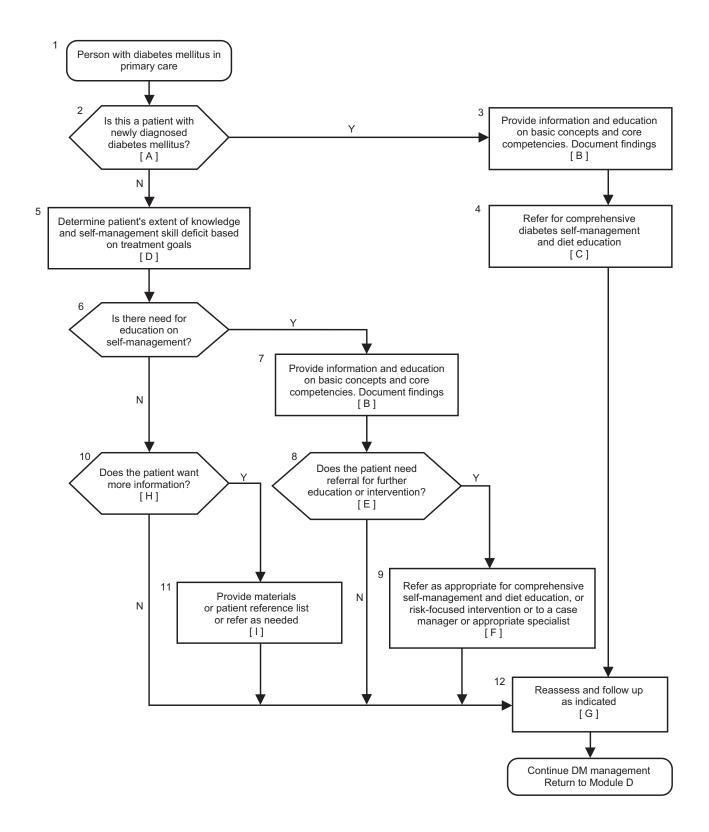


Table M1: Recommendations for SMBG		
Recommendations for SMBG		
Patients on Oral Agents	For stable type 2 DM: no more than 50 strips per 150 days. This allows for twice-weekly testing. An increased number of strips may be needed for a limited time period for the following indications: • Initiation of therapy and/or active adjustment of oral agents, meal plan, or exercise/activity • Detection and prevention of hypoglycemia when symptoms are suggestive of such, or if there is documented hypoglycemia unawareness • Detection of hyperglycemia when symptoms or urine glycosuria (for the occasional patient using urine test strips) are suggestive of such	
Patients on Insulin	 The frequency of monitoring should be individualized based on the frequency of insulin injections, hypoglycemic reactions, level of glycemic control, and patient/provider use of the data to adjust therapy. A combination of pre- and postprandial tests should be performed, up to 4 times per day. 	